



DOCKET NO. 17349CIP (AP)
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of Chow, et al.

Serial No: 10/039,827

Filed: October 19, 2001

For: METHODS AND COMPOSITIONS FOR
MODULATING ALPHA ADRNERGIC
RECEPTOR ACTIVITY

Group Art Unit: 1614

Examiner: Fay, Z.

OCT 04 2004

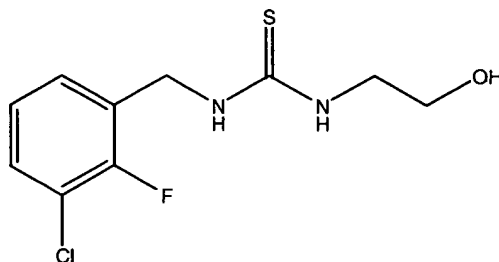
TECH CENTER 1600/2900

DECLARATION OF DANIEL GIL, Ph.D.

Dear Sir,

I, DANIEL GIL, Ph.D., hereby declare as follows:

1. I hold the title of Senior Research Investigator at Allergan, Inc. I have worked in the Department of Biological Sciences at Allergan for 16 years.
2. I am an inventor of the subject matter of the present patent application.
3. I am aware that claims 1-3, drawn to a single compound having the following formula:



and its esters and salts, have been rejected as allegedly obvious in light of a computerized printout provided by the Examiner of a Chemical Abstracts entry, Reiter et al., 93:532428. I have reviewed these claims and this Chemical Abstracts entry.

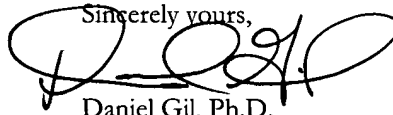
4. The Chemical Abstracts article discusses that a genus of compounds having "diuretic and saluretic activity" were prepared which include compounds of the formula:



Wherein R is an "optionally substituted" phenyl group., R₁ is H, Me, Et, Pr, CHMe₂, (CH₂)₆Me, or cyclopropyl; R₂ is H, Me, Et, Bu, cyclohexyl, CH₂CH₂OH; AND R₃ IS (CH₂)₃OH, CH₂CHMeOH, CH₂CMeOH, CH₂CMe₂OH, CHEtCH₂OH, allyl, CH₂CMe=CH₂, CHEtCH₂.

5. When conducting the experiments set forth in Examples 2-5 of the specification, the claimed compound was administered to groups of rats and cynomolgus monkeys. For example, Example 5 indicates that rats were administered doses of 1-(3-chloro-2-fluorobenzyl)-3-(2-hydroxyethyl)-thiourea (FORMULA 2) ranging from 1 to 300 micrograms/kg i.p., and at 0.1, 1 and 3 mg/kg. See specification at page 23, lines 24-32. Greater than 80% analgesic activity (reversal of allodynia) was observed at an i.p.dose of 10 ug/kg, and at an oral dose of 0.1 mg/kg, and no significant diuretic activity was observed at these dosages when urine volume was assessed.
6. Accordingly the above-described evidence clearly indicates that 1-(3-chloro-2-fluorobenzyl)-3-(2-hydroxyethyl)-thiourea lacks diuretic activity at analgesically relevant dosages.
7. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Sincerely yours,

A handwritten signature in black ink, appearing to read 'D. Gil', with a stylized flourish at the end.

Daniel Gil, Ph.D.
Senior Research Investigator